MALARIA IN INDIA — IS AN ECOFRIENDLY SOLUTION POSSIBLE?

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Malaria control is complicated by the existence of vector species, sometimes morphologically indistinguishable, but having very different ecology and behaviour. Early attempts to control malaria by eliminating breeding met with mixed success. In Mumbai city, however, malaria transmission was completely eliminated for many years using simple anti-larval measures. The advent of residual spraying with DDT led to a dramatic reduction in malaria all over the country, but development of resistance, together with administrative problems, resulted in resurgence. Though the cases have now levelled off, numbers are still too high for complacency, and the proportion of *falciparum* cases is on the rise. More potent than DDT and far less damaging to the environment are the synthetic pyrethroids. Pyrethroid-treated bed-nets have been particularly successful, reducing malaria incidence significantly in a variety of rural situations. The amount of insecticide used is very small in comparison with house spraying, making the method cost-effective. This technology, now undergoing large-scale trials, promises to be the main plank of the malaria control strategy.

INTRODUCTION

Lizards, birds, rodents and primates, all harbour various species of the protozoan parasite *Plasmodium*, which cause malaria and are transmitted to vertebrate hosts by mosquitoes. *Plasmodium* species are often group-specific; the species found among primates are, naturally, of most interest to us. Four species cause disease in man, *P. vivax, P. falciparum, P. malariae* and *P. ovale*, of which only the first two are common. Several species are found in non-human primates, including *P. inui* in *Macaca radiata* in the Nilgiri foothills. None of these infect man, and there is only one monkey, the owl monkey *Aotus trivirgatus* of South America, which can be infected experimentally with human malaria. Interestingly, however, *P. rodhaini* of chimpanzees is morphologically identical with *P. malariae* of man (Bruce-Chwatt 1980), which shows that when the hominids split off from chimpanzee stock in Africa around 7-8 million years ago, the association with malaria was already there. New and exclusively human species must have evolved along with the hominids. Mosquitoes have, of course, been around for very much longer, and fossil mosquitoes have been found in 30 million year old geological strata.

Malaria is a disease which has caused tremendous suffering, and social and economic losses to mankind through the ages. It still remains one of the leading causes of sickness and death in the developing world, causing 300-500 million cases and 1.5 to 2.7 million deaths per year (WHO sources). The early symptoms of malaria are well known: intermittent high fever, accompanied by chills and violent shivering. Malaria caused by *P. vivax* is very debilitating, with the patient suffering a series of relapses if not treated, but it is rarely life threatening. *P. falciparum* malaria, on the other hand, if misdiagnosed or untreated, can result in cerebral malaria, leading to death. The patient becomes comatose and may also develop renal haemorrhages and other complications. Pregnant women and children are the most vulnerable to anaemia caused by malaria. In areas of high malaria transmission some degree of immunity develops, and unhealthy children with big bellies and large spleens used to be a common sight in the tea gardens of Assam.

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Mosquitoes and Malaria

It was Sir Ronald Ross who first saw, in Secunderabad on August 20, 1897, the malarial parasite on the stomach wall of a female *Anopheles* mosquito collected from the mosquito net of a patient with malaria. He later demonstrated that bird malaria was transmitted from sparrow to sparrow by the bite of an infected mosquito; while Bignami, Bastianelli and Grassi in Italy showed subsequently that human malaria was also mosquito-borne. The implications of these findings were immediately clear — mosquito control would automatically control malaria. At that time little was known about the mosquitoes of India. In 1900, Colonel G.M. Giles read a paper before the Bombay Natural History Society, in which he said "Two years ago when I took up the task of collecting the history of the Culicidae...no more than four species were recorded as having been found in all India. There was in fact hardly any known country with such scanty records of the subject."(Covell 1952). Extensive surveys were carried out during the next three decades, which would result in two volumes of the Fauna of British India series on mosquitoes, one on the Anophelini and the other on the Culicini, which have provided a solid basis for much of the great quantity of basic and applied research that has followed. Between 1901 and 1930, ten papers on mosquitoes and malaria were published in the *Journal of the Bombay Natural History Society*, and these are listed by Covell (1952). Today 365 species of mosquitoes have been recorded from India.

Only the genus *Anopheles* can transmit human malaria. There are 59 species on the Indian list today, of which 8 have been incriminated as major vectors (*A. culicifacies, A. stephensi, A. fluviatilis, A. minimus, A. dirus, A. sundaicus, A. annularis* and *A. philippinensis*). Six other species are considered to be secondary vectors in localised areas (Ramachandra Rao 1984).

A. culicifacies is probably the most widespread rural vector, and also plays a role in the outlying suburbs of major cities, such as Delhi. This species breeds in pools and the slow-flowing water at the grassy edges of streams and rivers. It is quick to adapt to man-made breeding sites, and has been the main incidental beneficiary from irrigation projects over the country. Thus it breeds prolifically in pools within irrigation canals and channels when water is not actually flowing in them, in rainwater standing in rocky hollows exposed in dry riverbeds created by dams, in borrow pits and seepages from canals, and to some extent in fields newly planted with rice[1]. However, there was always a puzzling lack of correspondence between the distribution and population density of this species and the prevalence of malaria. In recent years it has been shown that taxa once believed to be a single species are in fact groups of sibling species, which are morphologically identical but which can be separated by cytological techniques. Five sibling species are known in *A. culicifacies* in India, named species A to E. Two or more sibling species may be sympatric, and sterile hybrids are found in nature. All the sibling species are zoophilic, i.e. they prefer to feed on cattle rather than on man, but the relative degree of feeding on man varies considerably. Species B rarely feeds on man, while species A and sometimes C in northern India and species D and E in southern India do so relatively frequently. It is no surprise, therefore, to find that the last four are potent vectors, and many infective individuals have been found in dissections of wild-caught females. B is a poor vector, if at all, and only one wild-caught female, reliably identified as species B, has been found to be positive for the malarial parasite (Suguna *et al.*

[1]*Anopheles culicifacies* is generally regarded as a rice-field breeder, mainly on the basis of studies in the 1930s in Pattukotai district in Tamil Nadu. However, many recent studies in the same and other parts of Tamil Nadu have shown that the species is not breeding extensively in this habitat.

1983) in several long series of dissections. *Anopheles culicifacies* s.l. is not a vector in forested areas, but is known to replace other vector species in the wake of deforestation in the Western Ghats (Tewari *et al.* 1987). In Orissa, another species, *A. fluviatilis* was found to transmit malaria in forest villages, where *A. culicifacies* species B and C were also present but not feeding on man. In deforested areas where *A. fluviatilis* had been replaced by *A. culicifacies* species A, this was the main vector (Nanda *et al.* 2000). Surveys in 3 topographically different areas in Uttar Pradesh showed a good correlation between sibling species composition in the population of *A. culicifacies* and malaria incidence. Sibling species A, B, and C coexisted here, and where the proportion of the non-vector species B greatly exceeded the other two, malaria endemicity was low. Conversely, in a zone of high malaria transmission, the population of A and C together was about the same as B (Tiwari *et al.* 1994).

A. stephensi is the major vector of malaria in urban areas. This species has adapted to the peri-domestic environment, and breeds freely in domestic wells, water-storage containers, concrete cisterns and overhead tanks. It also breeds in ponds and streams in rural areas of northern and peninsular India, but apparently not in Tamil Nadu, where several long-term studies have confirmed that it is confined to small towns and cities, and is absent from villages even in malarious areas. No sibling species have been described in *A. stephensi*, but the rural form has been separated on the morphological characteristics of the egg as variety *mysorensis*. In the environs of Delhi, a form has been described intermediate between the type and variety *mysorensis*.

A. fluviatilis is a widespread and dangerous vector of foothills and forests. It requires flowing water to breed, and thrives along the grassy verges of forest streams. Three sibling species have been described, named species S, T and U. Here too the blood-feeding habits of the various sibling species determine their capacity to transmit malaria. Thus, in Orissa sibling species S was strongly anthropophilic (man feeding), and in villages where it was dominant it was the major vector (Nanda *et al.* 2000). Species T and U are zoophilic, and in the Bhabar and Terai of Uttar Pradesh where they are sympatric, they are poor vectors, and other vector species transmit malaria (Shukla *et al.* 1998).

A. minimus also breeds in streams and water channels, and is the main vector of the northeastern states. It also transmitted malaria in the Bhabar and Terai, but in the early years of the National Malaria Eradication Programme it disappeared. After the clearing of this belt for agriculture, it has been largely replaced by *A. culicifacies* s.l. and *A. fluviatilis* s.l.

A. dirus is another vector species in which 7 sibling species have been described in south and southeast Asia. Two of them occur in India, sibling species D, which is a major vector in the northeastern zone, and the rare species E in the forests of Wynaad, in southwestern India. These species breed in undisturbed deep forest in pools and in transient rainwater collections like elephant footprints.

A. sundaicus breeds in brackish water, and was once an important vector in coastal areas of Bengal and Orissa, from which it seems to have disappeared. It is, however, an important vector in the Andaman and Nicobar Islands. *A. annularis* transmits malaria in Assam, Bengal and coastal Orissa and *A. philippinensis* in deltaic Bengal, Assam and Meghalaya.

The varied habits of malaria vectors in different parts of the country greatly complicate control efforts.

Control of Malaria

Early attempts to control Anophelines

There was at best mixed success for early attempts to reduce the incidence of malaria. Simple methods were used, such as draining and filling anopheline breeding-sites in shallow standing water, and treating others which could not be removed with kerosene. It was soon realized that since mosquitoes could fly from a distance of at least 3/4 of a mile, control efforts must be undertaken simultaneously over large tracts. Generally, anopheline breeding in rural tracts was diffused over vast areas, and frequently it was found that the amount of organisation, supervision, labour and expenditure involved made control impracticable. Some successes were documented, mainly in places in which economic interests were involved, notably at dam sites. In such situations, minor engineering work could remove unnecessary stagnation of water, and canals could be lined with concrete to prevent seepage. Without these measures and the early detection and treatment of malaria cases among labour, it would have been impossible to complete such projects. In the tea gardens of Assam, breeding of the vector *Anopheles minimus* in water channels was prevented by growing shade bushes along them. This prevented the growth of grass along the edges, which proved to be critical for the breeding of this species. Mosquito screening of labour lines also helped to reduce the loss of man-days due to fever.

The great success story of this period was, however, the control of malaria in Bombay (= Mumbai). This city was always considered to be unhealthy, and a blood survey in 1911 showed that 2,542 fever cases among the City Police were caused by malaria. Bentley (1911) found that *A. stephensi* was responsible. Since this vector breeds in easily located and well defined breeding sites, he thought malaria could be controlled here more easily than elsewhere by permanently closing domestic wells and installing pumps, filling up unwanted wells, and making overhead tanks (the other major source of vectors) mosquito proof. Ornamental ponds and fountains were stocked with larvivorous fish. Bentley and his successor Captain Chalam, managed to keep parts of Bombay relatively free from malaria. It was, however, Major Covell (1928) who organised the work and made detailed recommendations including penal provisions of the Municipal Act for those who did not cooperate. He also succeeded in getting sanction for a permanent staff for malaria control, facilitated reportedly because the Governor of the state came back from a hunting trip and fell ill with malaria (Ramachandra Rao 1984). The result was the complete elimination of malaria transmission, with the only cases reported in the city being imported from outside.

However, this example and the partial successes elsewhere remained localised and had little impact on the larger problem of malaria in the country.

The DDT era

The discovery of the residual insecticidal action of DDT made it possible to target the adult anopheline female mosquito, which rests on walls and ceilings after feeding and can pick up a lethal dose of insecticide. Pilot studies were very encouraging, and a National Malaria Control Programme (NMCP) was launched in 1953. This was so successful in reducing malaria incidence that the programme was converted, in 1959, into the National Malaria Eradication Programme (NMEP), rightly described as the single largest public health programme in the world. It received technical support from WHO and donor support from international agencies.

Meanwhile, there were warnings. In 1962, Rachel Carson published her book *Silent Spring*, highlighting the damage caused to the environment by large-scale pesticide use. This led to a complete ban on the use of organochlorines for agriculture, but exempted the use of DDT for public health use. Spraying within houses was considered minimally damaging to the environment, and links with cancer have not been confirmed in several carefully carried out epidemiological studies made since. Besides, in the '60s DDT was saving lives. While there was no adequate surveillance system before 1953, it was estimated that there were 75 million cases of malaria and 800,000 deaths each year in India. Numbers fell rapidly after control, till in 1965 only about 100,000 cases were reported, and no deaths. It is also important to remember that at that time the NMEP was an *eradication* programme, with a definite timeframe, and residual spraying was never intended to continue indefinitely. But after 1965 the setbacks began, and there was a resurgence, which reached a peak of around 6.5 million cases in 1976. Changes in strategy brought numbers down somewhat, but cases have stagnated at between 2 and 3 million annually, with about 1,000 deaths. The programme managers clung to the mindset of the eradication era long after it ceased to be useful. It was only in 1995 that there was a change of name to National Anti-Malaria Programme (NAMP).

The reasons for the resurgence of malaria have been discussed and analysed many times: technical factors such as the development of resistance to insecticides, administrative failures including inadequate planning, shortage of funds and staff, and poor training of personnel. It has to be remembered, however, that in spite of the setbacks, malaria incidence has not returned to the previous level. Nevertheless, there is little cause for complacency, since under-reporting is a serious concern. Though the official figures show that at present numbers of cases are between 2 and 4 per cent of the pre-control level, the correct figures may be between five and fifteen times higher (SEARO 2000). Under-reporting of deaths is still more serious. Scientists of the Malaria Research Centre, Delhi, believe that only 1 in 200 malaria deaths is being reported. Even more disturbing is the increasing proportion of cases caused by the malignant *Plasmodium falciparum.* In 1970 about 14 per cent were caused by this species, but by 1999 the proportion was 50 %.

Changes in land usage have sometimes contributed to the problem. For example, the Thar Desert region was formerly only mildly prone to malaria, transmitted by *Anopheles stephensi* breeding in traditional water storage reservoirs. Following the introduction of canal irrigation and cultivation over wide areas, *A. culicifacies* has established itself. Between 1961 and 1994, total malaria incidence as well as *falciparum* malaria has increased 3.5 times (Tyagi *et al.* 1995).

Urban areas were not sprayed with DDT and other insecticides. In many towns urban malaria schemes, based on the Bombay model and paid for by municipalities, were implemented with varied success. In Bombay itself, control remained exemplary with strict implementation of the Municipal Act and good supervision until comparatively recently. Most of the credit for this belongs to P. B. Deobhankar, Insecticide Officer of the Municipality. After he retired in the early 1990s, the system appears to have broken down and indigenous transmission of malaria is on the rise. Damaged overhead tanks in old buildings and water storage drums in slums provide breeding sites. However, most of the cases occur in association with construction sites. *A. stephensi* is quick to breed in the small cisterns which are built and filled with water used for pouring over fresh concrete structures. These are not emptied for long periods, nor does the builder now fear inspection and prosecution. The source of malaria infection is usually migrant labour at construction sites. A focus of transmission quickly develops, which will shift to another site when building is completed.

Where do we go from here?

At the beginning of the 21st century, we face a deteriorating malaria situation, with high levels of resistance to DDT in vector mosquitoes, and also widespread resistance in humans to chloroquine (the frontline drug for treatment) besides prospects of rapid development of multi-drug resistance to other common drugs. All the same, Dr. Gro Harlem Brundtland, Director General of WHO, plans to halve malaria mortality by 2010, and again halve it by 2015. There is no major breakthrough in technology, but the new strategy stresses flexibility, political commitment and resource mobilisation to deploy existing techniques with improved organisational skill (SEARO 2000).

One of the most hopeful research developments of recent times has been the treatment of bed-nets with synthetic pyrethroids, to protect communities from mosquito bites. Pyrethroids have a chemical structure based on the natural product pyrethrum, and combine the advantages of a more powerful insecticidal action and very low mammalian toxicity. Permethrin, deltamethrin and lambdacyhalothrin are among those which have been used for this purpose. An untreated bed-net gives protection only as long as it remains without holes. A treated net with holes, however, will drive away blood-seeking mosquitoes because pyrethroids have an irritant and repellant effect, and will also kill those which rest on it for long enough to acquire a lethal dose. If the whole community sleeps under insecticide treated nets (ITNs) there will be a significant impact on malaria transmission.

This technology was tested in Assam, where *Anopheles minimus* was a suitable target because biting peaked around midnight, a time when it is possible to protect people with nets. Treated nets were distributed in 3 villages, untreated nets in others and yet others served as controls. They were well accepted by the tribal population. The nets provided a high degree of personal protection from mosquito-bite, while in the villages with ITNs the population of *A. minimus* was also reduced. Malaria incidence was monitored weekly, and rose significantly in the control villages during the study, while remaining at the same level in villages with untreated nets. In villages with ITNs however, there was a significant decline (Jana-Kara *et al.* 1995). In a larger trial covering 126 villages in Gujarat, house spraying with deltamethrin was compared with nets treated with the same insecticide. Here the vector was *A. culicifacies* species A. Again there was significantly lower incidence in ITN villages than in sprayed villages, and both were significantly better than villages without any interventions (Misra *et al.* 1999). These results are very similar to those obtained in other parts of the developing world (Curtis and Mnzava 2000). Thus, ITNs could be of use in an integrated programme of control in both these areas.

But the real test of ITN technology in India is among the adivasis of Orissa, who live in areas where the health infrastructure is weakest, and where malaria control made no impact because residual spraying was never socially acceptable to the people. In parts of Orissa, villagers wait patiently till spraying is over, and then start mud-plastering their walls to cover the unsightly white stains left by DDT. Yet the spraying is carried out regardless each year. Orissa accounted for about 20 % of all malaria cases in India, 38 % of all the *falciparum* and 55 % of all malaria deaths reported in 1991. Two studies have been carried out which have shown striking reduction in populations of the vector, *A. fluviatilis* species S, due to the use of ITNs (Jambulingam *et al.* 1989 and Yadav and Sampath 1993). These were followed by a Social Marketing Project in Keonjhar District run by the Government of Orissa, the British Council, CARE and the Malaria Research Centre. This sought to help communities to generate demand for nets and run their own malaria control projects. Dr. John Oommen, working in the Community Health Department of a small hospital in Rayagada District in Orissa, which provides primary health care to a population of over 10,000 in 46 villages, has taken this approach still further. The Bissam Cuttack Block, where this hospital is situated, is one of six blocks in Orissa which showed a negative rate of growth in the 1991 census, with deaths outnumbering births. Fever was the single largest cause of death, particularly in the under-five age group. Many of these deaths occurred at home and no blood smears were obtained, but it is very likely that they were due to malaria. Dr. Oommen works to set up a people's movement against malaria. Through 1996 and early 1997, 38 villages opted for malaria education and for ITNs, which they paid for by instalments, convinced that the economic losses due to malaria outweighed the cost of the nets. Hospital records showed that in 1997 fever cases had dropped by 36%, fever deaths by 40% and hospital admissions for malaria by 39% by comparison with the previous year (Oommen *et al.* 1999). Overall child mortality due to any cause also fell to about half (Dr. J. Oommen, pers. comm.). The reason for this is that malnourished children with malaria have a lowered resistance to other infections as well[2]. Much larger trials involving NGOs, research organisations and the District administration, are now underway in Malkangiri and Gajapati districts in Orissa.

Clearly, nets have an important role to play in an integrated vector control programme, but they will not be suitable in situations where malaria transmission takes place mainly outdoors, or early in the night. Can the technology be made cost effective? DDT is still the cheapest insecticide but is no longer effective in reducing malaria to acceptable levels. Malathion is 3 to 4 times more costly, though more effective in controlling vectors, but coverage declines due to refusals because of its unpleasant smell. Synthetic pyrethroids are very effective but somewhat more costly than malathion. If ITN technology can be made effective the cost will be less than that of DDT spraying (SEARO 2000), because less insecticide is required per household to treat nets. Optimal results depend on the mass effect on vector populations rather than personal protection of those sleeping under nets. While people are often willing to pay the initial cost for ITNs, they are reluctant to pay the additional cost of annual re-treatment. Curtis and Maxwell (2002) believe that the full potential of the method can best be achieved if insecticide treatment is provided free, citing the example of Vietnam, where 11 million people are now protected by treated nets, and insecticide is provided free as a public health service. A major decline in malaria incidence has resulted [Tran Duc Hinh 2001 (www.Mekong-malaria.org/meis/mmf6/mmf6 15htm) in Curtis and Maxwell 2002]: one of the few successes of malaria control on a national scale in recent times.

Since there is a strong likelihood that resistance to pyrethroids may develop as a result of widespread use of treated nets, non-pyrethroid alternatives with low toxicity, for example carbosulphan, are already being tested for treating nets. Early results suggest that non-irritant insecticides, which do not repel mosquitoes, may kill more efficiently than pyrethroids and therefore result in much better control of malaria than before (Curtis, in press). Encouraging as these developments are, ITNs should be only one component in an integrated programme.

Does indoor residual spraying still have a role? Today, there appears to be little justification for the continued use of DDT in India. But there are some African countries and parts of Latin America with a heavy burden of malaria, in which it can still save lives. Considerations like these led to the resolution of the International Convention on Persistent Organic Pollutants in December 2000, which allowed the continued use of DDT for vector control in 28 countries, provided that WHO guidelines were strictly followed. These countries are also expected to develop alternatives, and their progress towards this objective is to be reviewed after 3 years.

In India, bio-environmental control, including source reduction, is still the method of choice wherever anopheline breeding sites are well defined and accessible, as they are in urban areas. Larvivorous fish such as *Gambusia*, *Tilapia* and some of the carps, have proved their worth in wells, pits and ornamental tanks, and an added advantage is that edible fish can be sustainably harvested to add to family or

[2] Reduction in overall childhood mortality as a result of community use of ITNs has been well documented in several studies in Africa.

community income. *Bacillus thuringiensis* var. *israelensis* has not been extensively used in India. While it kills anopheline larvae effectively, it does not cycle in nature, and therefore recurrent re-treatment of breeding sites is necessary. Still a long way in the future is the possible replacement of natural populations of vectors by transgenic mosquitoes into which a gene for refractoriness to malaria has been inserted. Such a gene has been found, and modified mosquitoes feeding on malaria-infected mouse blood are 80% less likely to have malaria in their salivary glands, and they are almost totally unable to pass on malaria to other mice (Ito *et al.* 2002). However the resistance gene for human malaria may not be the same, and in any case great caution would have to be exercised before genetically modified mosquitoes could be released into the environment.

In conclusion, there is one important lesson of the India experience that needs to be emphasized — that vector control which is also environment friendly is practicable. But in addition to research, good management is a prerequisite for major success. Covell and Deobhankar were outstanding managers within the government system, while the potential of the NGO sector is now being demonstrated by Oommen and others. There is real hope that these successes can be replicated, and that malaria can be effectively controlled without the release of toxic chemicals into the environment.

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